

PERSPECTIVE ARTICLE

Beyond defense: Immunity as an evolutionary network for preserving biological organization from microbes to complex life

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Abstract

Biological evolution has produced increasing organizational complexity, from molecular systems to integrated multicellular organisms. Natural selection explains why advantageous variation persists, but sustaining increasingly complex living systems also requires mechanisms that preserve functional organization while allowing continual adaptive change. We propose that immunity is one of the principal networks providing this continuity: rather than serving solely as pathogen defense, it functions as an evolved recognition-and-regulation system that shapes compatible relationships across linked cellular, tissue, organismal, and host-associated ecological levels. Here, a compatible relationship is one that, within a defined biological context and timescale, sustains or can be regulated to restore system-level function; compatibility does not imply permanence, harmony, or the absence of conflict. Drawing on immunology, microbiology, evolutionary biology, developmental biology, and host-microbiome research, we argue that the progressive refinement of biological recognition has let increasingly complex organisms maintain functional coherence amid genetic variation, microbial interactions, developmental remodeling, and environmental change. Host defense, immune tolerance, tissue homeostasis, inflammatory regulation, and host-microbiome interactions are complementary expressions of this broader organizational function, which preserves biological integrity while accommodating innovation. Compatible biological relationships thus supply the organizational context in which complexity can accumulate, integrate new functions, and persist over evolutionary time. This is not a new mechanism of evolution, but an organizational principle unifying established findings across disciplines, positioning immunity as an important contributor to the preservation of biological organization during the continued evolution of complex life.

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Citation: Stefano GB. Beyond defense: Immunity as an evolutionary network for preserving biological organization from microbes to complex life. *Microbes & Immunity*. doi: 10.36922/MI026290086

Received: July 15, 2026

Revised: August 10, 2026

Accepted: August 11, 2026

Published online: August 19, 2026

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Keywords: Immunity; Evolution; Biological organization; Chirality; Host-microbiome interactions; mirror microbes; SpudCells

1. Introduction

Life is commonly viewed as the progressive evolution of increasing biological complexity, from simple molecular systems to multicellular organisms. Yet each increase in complexity also creates new opportunities for organizational instability.¹

Persistence of complex life therefore depends not only on generating biological novelty but on evolving mechanisms that preserve functional organization while permitting continual adaptive change.^{2,3} For clarity, organizational continuity refers to persistence of essential function through change; organizational integrity to retention of system identity and boundary conditions; functional coherence to coordinated operation among components; and organizational stability to the regulated capacity to remain functional despite perturbation.

Immunity occupies a unique position among these mechanisms. Traditionally viewed as the system distinguishing self from non-self and protecting against infection, immunity is now recognized as contributing to tissue homeostasis, development, metabolic regulation, repair, microbial symbiosis, and physiological integrity. This indicates that immunity is more than a defensive system: it continuously regulates the biological relationships that determine which interactions are preserved, modified, tolerated, or eliminated as organisms develop, adapt, and evolve.^{1,4–8} Operationally, a relationship is compatible when, within a specified biological context and timescale, it supports or does not materially impair measurable system-level functions and is therefore retained, tolerated, or adaptively modified by regulatory processes. Persistent functional disruption accompanied by containment, exclusion, or elimination is evidence of incompatibility.^{4–6}

This broader perspective is especially clear in evolutionary context. Long before vertebrate adaptive immunity emerged, living systems needed mechanisms to distinguish compatible from incompatible biological interactions. Primitive recognition systems among molecules, cells, and microorganisms promoted functional organization by favoring interactions that enhanced persistence while limiting those that disrupted biological integrity.^{1,8} As complexity increased, these processes evolved into progressively more sophisticated regulatory networks capable of preserving organization without constraining evolutionary innovation (**Figure 1**).^{4,6,9,10} The framework therefore does not equate every form of molecular or cellular recognition with immunity. Pre-immune recognition is treated as an evolutionary antecedent and constraint, whereas immunity is reserved for evolved recognition-and-regulation systems that deploy immune effectors to alter outcomes at cellular, tissue, organismal, or host-associated ecological levels.^{4,6,9,10}

The central question here extends beyond immunity's conventional functions: how has increasing biological complexity remained organized enough to permit continued evolutionary innovation? Immunity can be understood as one of the principal biological networks

through which living systems preserve organizational continuity by regulating compatible relationships across levels of biological organization (**Figure 1**). Host defense remains essential, but within this framework it is part of a broader evolutionary process that stabilizes organization while permitting continual adaptation—an organizational lens through which established findings across immunology, microbiology, evolutionary biology, and systems biology can be understood as parts of a coherent evolutionary process (**Figure 1**).¹⁰ Later sections therefore consider homochirality, mirror-life risk, and chemically defined synthetic cells as boundary cases rather than as immune mechanisms themselves. Their purpose is to test whether organizational continuity depends on conserved molecular compatibility and whether that dependence becomes visible when stereochemistry is inverted or living organization is synthetically minimized.

2. Microbial competition, biological recognition, and the evolution of organizational stability

Microorganisms dominated Earth's biosphere for most of evolutionary history and remain principal drivers of biological innovation.⁸ Continuous interactions among viruses, bacteria, archaea, and early eukaryotes generated selective pressures favoring increasingly effective molecular recognition, environmental sensing, communication, and adaptive response. Evolution therefore advanced not only through genetic variation but through the refinement of systems capable of organizing complex interactions while preserving functional integrity.^{10–13}

Although often viewed as conflict, microbial competition is also a powerful source of innovation through reciprocal adaptation. Bacteriophage–host coevolution, horizontal gene transfer, CRISPR-Cas defense, quorum sensing, and metabolic cooperation all show that evolutionary success depends on increasingly selective biological recognition: organisms able to distinguish compatible from incompatible interactions gained a substantial advantage, sustaining beneficial relationships while constraining disruptive ones.^{14,15}

Endosymbiosis illustrates this principle clearly. The incorporation of ancestral bacteria that gave rise to mitochondria, and later chloroplasts, required more than physical coexistence—it depended on stable molecular and regulatory relationships that allowed formerly independent organisms to function as integrated systems. Similar principles underlie multicellularity, host–microbe symbioses, and complex microbial communities: increasing complexity depended not simply on new components but on their successful integration into existing organizational networks.^{7,10,16–18}

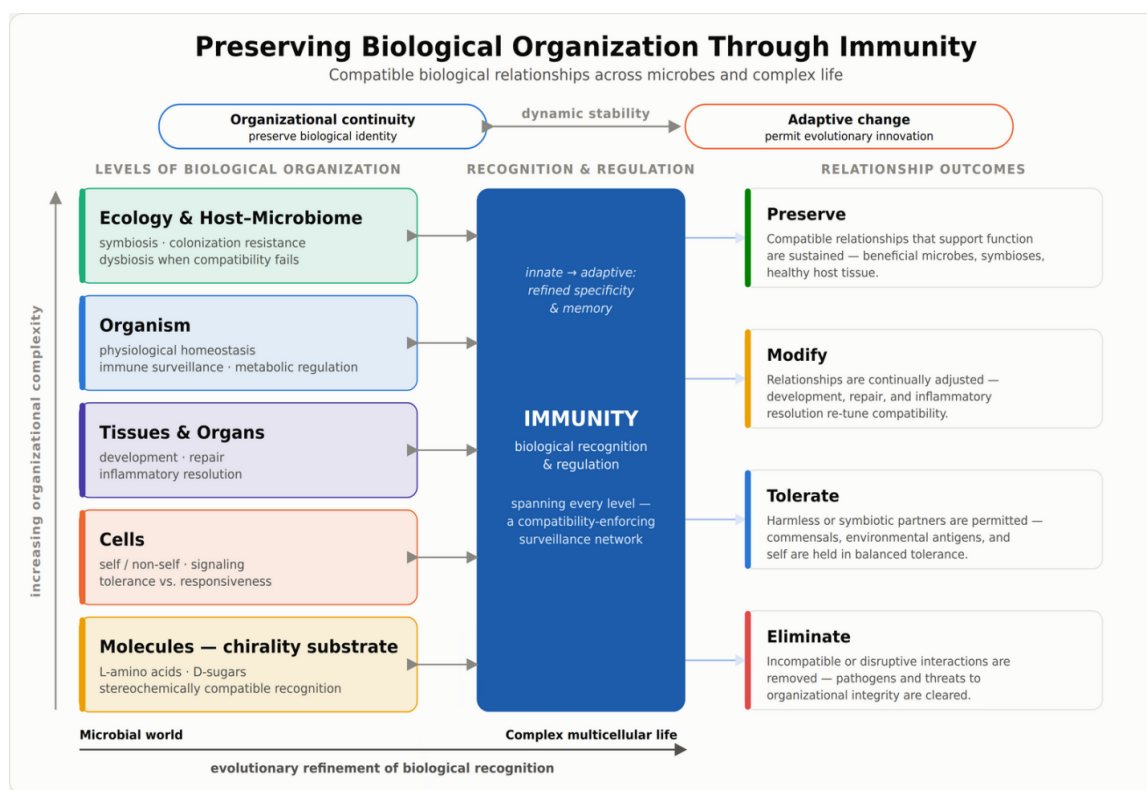


Figure 1. Immunity preserves biological organization through compatible relationships across levels, from microbes to complex life. Levels of biological organization are arranged by increasing complexity (left), from the molecular chirality substrate (L-amino acids, D-sugars) through cells, tissues and organs, the organism, and host–microbiome ecology. Immunity (center) is shown as a specialized recognition-and-regulation network whose molecular mechanisms act across linked cellular, tissue, organismal, and host-associated ecological levels; the chirality substrate is presented as a prerequisite for stereochemically selective recognition, not as an immune system in itself. Within these biological contexts, immune processes influence one of four relationship outcomes (right): interactions supporting function may be preserved or adaptively modified, harmless or symbiotic partners may be tolerated, and disruptive interactions may be eliminated. Together, these functions can contribute to the balance between organizational continuity and adaptive change (top), allowing compatible relationships to provide a context in which biological complexity accumulates, integrates, and persists.

Biological evolution thus reflects the progressive refinement of compatible relationships across levels of organization. Natural selection retains advantageous variation, but innovations persist only when successfully integrated into functioning systems without disrupting overall organization, providing the organizational context within which complexity can accumulate while remaining functionally coherent through evolutionary time.¹

This organizational principle extends naturally to immunity. Immune systems did not introduce biological recognition into evolution but represent its progressive specialization within increasingly complex organisms. As complexity expanded, recognition systems evolved into integrated regulatory networks capable of preserving biological identity while remaining adaptable to continual genetic, ecological, and environmental change. Immunity therefore emerged as one of evolution's most sophisticated

mechanisms for maintaining organizational stability while permitting continued adaptive innovation.^{1,19,20}

3. Immunity as the evolutionary architecture of biological recognition

Immune system evolution is usually framed as the progressive enhancement of host defense against pathogens, and abundant evidence supports this: immune systems identify pathogens, clear infected or damaged cells, maintain tissue integrity, and support organismal survival. Yet these activities share a deeper function—the continual recognition and regulation of biologically meaningful relationships. Recognition, not elimination alone, is thus the organizing principle of immune function.^{1,19,21,22}

Immunity rests on selective biological discrimination. Immune cells distinguish self from non-self, harmful from harmless, and transient from persistent interactions—

distinctions now understood to be dynamic rather than fixed. Immune systems continuously negotiate relationships with commensal microbes, symbiotic partners, environmental antigens, and host tissues, balancing responsiveness against tolerance, and therefore act less as a simple defense system than as a selective regulator of biological integration.^{23–25} This broader view spans modern immunology: beyond infection control, innate and adaptive immunity contribute to tissue development, repair, metabolic regulation, physiological homeostasis, and host–microbiome interactions, continuously sustaining the organizational relationships underlying normal biology rather than only responses to disease.^{1,5,26}

Mechanistically, the proposed organizational role is implemented through established immune pathways rather than through an abstract “compatibility judgment.” Pattern-recognition receptors and complement identify conserved microbial or damage-associated structures; antigen-receptor signaling, co-stimulation, and inhibitory checkpoints calibrate lymphocyte activation; regulatory T cells, cytokine networks, and inflammatory-resolution programs restrain or terminate responses; and barrier compartmentalization and mucosal immunoglobulin A permit commensal persistence while limiting tissue invasion. These pathways produce measurable outcomes—clearance, containment, tolerance, repair, or chronic inflammation—providing concrete causal routes by which immune recognition can preserve or disrupt biological organization.^{4,5,9,19,21,22,25,26}

The microbiome illustrates this clearly. Resident microbial communities support nutrient metabolism, epithelial integrity, immune maturation, and colonization resistance, and their persistence depends on immune regulation that neither eliminates beneficial microbes nor allows unchecked expansion; biological stability thus arises from maintaining compatible host–microbe relationships rather than from static equilibrium.^{1,5,17,27} Host–pathogen interactions show the complementary side of this principle. Pathogens continually evolve immune evasion, molecular mimicry, metabolic manipulation, and persistence strategies, while hosts refine recognition, inflammatory regulation, barrier function, and immunological memory in response—an ongoing evolutionary dialogue that progressively sharpens biological recognition.^{10,19,28}

Seen this way, immunity is one of biology’s most specialized organizational networks. Host defense, tolerance, tissue maintenance, inflammatory regulation, and microbiome homeostasis are not separate functions but complementary expressions of one goal: preserving compatible biological relationships while allowing

continued adaptive change. Immunity is thus not merely protective; it is a highly specialized evolutionary refinement of biological recognition that can help complex living systems maintain integrity while remaining capable of further evolution.^{1,8}

4. Compatible biological relationships and the organization of evolutionary complexity

Progressive increases in biological complexity present one of evolution’s central challenges. As organisms acquire new genes, regulatory pathways, specialized cell types, tissues, organs, and ecological interactions, they also generate an expanding network of biological relationships requiring continual coordination. Evolutionary innovation therefore depends not only on the appearance of advantageous biological variation but also on mechanisms capable of preserving functional organization as complexity increases.^{3,29,30}

Natural selection remains the primary mechanism through which advantageous variation is retained. However, evolutionary innovations persist only when newly acquired structures, signaling pathways, metabolic networks, and symbiotic associations become successfully integrated within existing biological systems. Adaptive variation alone is therefore insufficient; long-term evolutionary success requires both selective advantage and successful organizational integration.^{29,31}

This principle is evident throughout biological organization. Proteins function because their structures permit highly selective molecular interactions; cells preserve physiological integrity through coordinated communication among intracellular pathways, neighboring cells, and their extracellular environment; multicellular organisms arise through regulated developmental interactions; and host-associated microbial communities depend on continually maintained compatibility between host physiology and microbial ecology. Across every level, complexity persists because functional relationships remain sufficiently coordinated to preserve coherent biological function despite continual molecular turnover, environmental change, and evolutionary innovation.^{17,32,33}

Importantly, compatibility should not be interpreted as permanence. Living systems remain dynamic throughout development, physiology, ecological adaptation, and evolution, so compatible biological relationships are continuously regulated rather than statically maintained. This dynamic stability enables organisms to accommodate continual change while preserving biological identity; biological resilience consequently reflects the regulation of compatible relationships rather than resistance to change

itself.^{34,35} In this usage, dynamic stability is the maintenance of an acceptable functional range during change, whereas resilience is recovery toward that range after disruption.

Host–microbe and host–pathogen interactions provide the clearest demonstrations of this organizational principle. Resident microbial communities exchange metabolites, signaling molecules, and immunological information with their hosts, remaining beneficial only while reciprocal regulation preserves compatibility between host physiology and microbial ecology; when that compatibility is disrupted, dysbiosis, chronic inflammation, metabolic dysfunction, and disease may follow, and restoration of health frequently depends less on eliminating individual microorganisms than on re-establishing compatible relationships.^{5,26,27} Conversely, successful pathogens exploit compatible molecular interfaces that permit attachment, cellular entry, immune evasion, metabolic manipulation, and intracellular persistence, while hosts continually refine recognition systems that distinguish interactions supporting normal physiology from those threatening organizational integrity—a reciprocal evolutionary dialogue that progressively refines biological recognition while preserving the organizational stability increasingly complex living systems require.^{19,28}

Collectively, these observations indicate that compatible biological relationships provide the organizational context within which biological complexity can accumulate: living systems are stabilized not because their individual components remain unchanged, but because their relationships remain sufficiently coordinated to preserve functional coherence despite continual adaptation. Within this framework, immunity assumes broader evolutionary significance. Immune systems do not create compatible biological relationships; rather, they continuously evaluate, preserve, modify, or terminate them according to their consequences for organismal integrity. Host defense, immune tolerance, tissue repair, inflammatory resolution, and regulation of host–microbiome interactions therefore represent complementary expressions of a common organizational function, making immunity one of evolution's principal biological networks for preserving the compatible relationships upon which increasingly complex life depends.

Importantly, this organizational framework does not replace established evolutionary mechanisms. Mutation, natural selection, genetic drift, horizontal gene transfer, ecological competition, and developmental constraint remain the principal drivers of biological evolution. Instead, the present perspective emphasizes the organizational conditions under which these mechanisms generate durable biological complexity, so that evolutionary

innovation and organizational compatibility operate cooperatively, allowing increasingly complex biological systems to emerge, integrate new functions, and persist through evolutionary time.^{1,10,36}

5. Immunity as an evolutionary stabilizing network

Immunity is best understood as a continuously operating biological network that preserves organizational integrity while permitting adaptive change. This does not diminish immunity's defensive functions; it situates them within a broader evolutionary context in which recognition, regulation, and selective interaction jointly sustain the organizational continuity that increasingly complex living systems require.^{1,8,21,22,25} This stabilizing role spans multiple levels of organization. Molecularly, immune recognition relies on selective receptor–ligand interactions. At the cellular tissue levels, immune regulation coordinates communication, repair, inflammatory resolution, and homeostasis. At the organismal level, immunity maintains dynamic relationships with resident microbiota while responding to environmental challenges. Across these linked levels, immunity often functions not only by eliminating threats but also by regulating the relationships on which normal function depends.^{5,26}

This multilevel organization reflects a core property of living systems: coherence is maintained through regulatory interactions operating simultaneously across nested hierarchical levels, from molecules to cells, tissues, organs, organisms, and ecological environments. Immune regulation can couple events across these linked levels, so that local recognition and effector activity influence broader tissue, organismal, and host–microbiome outcomes without implying that immunity governs every form of biological organization.^{1,34,35} Immunity's evolutionary history shows this organizational role being progressively refined: conserved innate mechanisms established early recognition systems, and adaptive immunity later expanded their specificity and memory without replacing their underlying function. Greater immunological sophistication thus reflects the refinement of biological recognition, not the emergence of a new strategy.^{4,20,22}

Collectively, these observations suggest two limited ways in which immunity can contribute to evolutionary persistence. First, immune regulation can preserve existing organization under changing environmental and microbial conditions. Second, by reducing otherwise disruptive interactions, it can help create conditions in which adaptive innovations remain viable. These claims concern contribution, not direction: immunity neither generates

variation nor determines which innovations arise, and its effect must be demonstrated through specific mechanisms and measurable outcomes.

Three recent developments provide boundary cases for, rather than direct proof of, the proposed framework. Gaut and colleagues' 2026 "SpudCells"—synthetic cells built from non-living, chemically defined components that nonetheless replicate, grow, feed, divide, and undergo Darwinian selection—show that organizational continuity and heritable variation can coexist in a self-replicating system without an evolved immune apparatus.³⁷ This separates the general requirement for organized persistence from the specific contribution of immunity in natural organisms. The near-universal use of L-amino acids and D-sugars identifies a conserved stereochemical constraint on molecular recognition, which Ozturk and Sasselov trace to homochirality propagating outward from the genome through a coupled prebiotic network.³⁸ Adamala and colleagues' warning that mirror life might evade ordinary immune recognition illustrates a mechanistically grounded prediction: reversing molecular handedness could disrupt receptor–ligand binding and effector recognition that evolved within the existing chiral biosphere.³⁹ These cases do not establish that immunity causes complexity; instead, they clarify the framework's boundaries by distinguishing a general organizational requirement, a molecular constraint on recognition, and the specialized surveillance functions of immune systems.

This interpretation remains fully consistent with established evolutionary biology: mutation, natural selection, genetic exchange, ecological competition, and developmental constraint remain the principal mechanisms of diversification. The present framework addresses a different question—the organizational conditions under which their products can remain functionally integrated—and positions immunity as one network that can contribute to continuity while evolution proceeds through those established mechanisms.

6. Discussion

The present opinion examines immunity from a perspective beyond its established role in host defense, while remaining grounded in contemporary immunology, microbiology, and evolutionary biology. Rather than proposing a new evolutionary mechanism, it identifies an organizational principle recurring across biological disciplines: immunity is best understood as one of the principal networks through which living systems preserve organizational integrity while remaining capable of continual adaptive evolution.^{22,25,26}

Organisms have evolved amid persistent microbial

competition, ecological change, and genetic variation. Under these conditions, increasing biological complexity required not only advantageous traits but also mechanisms capable of preserving functional organization amid molecular turnover, developmental remodeling, and environmental adaptation; evolutionary success thus reflects both the generation of novelty and the maintenance of organizational continuity.^{3,29,30}

Viewed in this light, biological recognition is broader than immunity and operates in molecular interactions, cellular communication, development, and ecological association. The narrower claim advanced here is that immune systems are a specialized subset of these recognition-and-regulation processes: within cells, tissues, organisms, and host–microbe interfaces, they help preserve, modify, tolerate, or eliminate interactions according to their functional consequences. This distinction prevents the framework from treating all biological recognition as immune activity.^{24,32,33}

This framework therefore emphasizes compatible biological relationships as the organizational context in which established evolutionary mechanisms generate durable complexity. It does not alter the accepted roles of mutation, natural selection, genetic drift, horizontal gene transfer, ecological competition, or developmental constraint, but highlights the conditions permitting these mechanisms to produce increasingly complex, adaptable systems.

This perspective also offers a useful direction for future research. Advances in systems biology, evolutionary immunology, microbiome science, structural biology, and computational modeling increasingly allow biological organization to be examined across hierarchical levels simultaneously, potentially clarifying how recognition networks coordinate compatible relationships during development, physiology, aging, ecological adaptation, and disease. Though conceptual, this framework generates experimentally testable questions about the evolution and maintenance of biological organization.^{34,35} Examples include whether disruption of a defined recognition pathway converts a previously tolerated host–microbe relationship into inflammatory pathology, whether restoration of regulatory signaling re-establishes functional compatibility, and whether stereochemical inversion predictably impairs immune binding or effector activation. Failure of such interventions to alter the proposed outcomes would constrain the framework.

Several limitations apply. This organizational interpretation is a conceptual synthesis rather than a comprehensive mechanistic model; many of the relationships discussed remain incompletely understood,

and causal interactions vary among organisms and evolutionary contexts. It should not be read as implying that compatibility alone explains biological complexity or that immune regulation governs all biological organization, but rather as an integrative lens through which observations across disciplines may be viewed within a coherent evolutionary framework. Accordingly, the framework is testable at the level of specified relationships, pathways, contexts, and outcomes; it is not a universal claim that immunity governs all biological organization. Analogies to pre-immune recognition are used to identify evolutionary continuity, not to assign immune causation where immune mechanisms are absent.

7. Conclusion

Taken together, immunity may be understood as substantially more than a biological defense system. The evidence considered throughout this paper suggests that, within multicellular organisms and host-associated ecosystems, immunity functions as one important recognition-and-regulation network through which organizational integrity can be preserved during adaptive change. More broadly, compatible biological relationships provide the organizational context within which biological complexity can accumulate, integrate new functions, and persist despite continual environmental and evolutionary change. This perspective does not propose a new mechanism of evolution; instead, it identifies an organizational pattern that has long been visible across multiple biological disciplines but has rarely been articulated as a unified evolutionary framework. Viewed in this way, immunity occupies a central position within the biological organization, not because it directs evolution, but because it helps preserve the organizational continuity upon which adaptive evolution ultimately depends.

Acknowledgments

None.

Funding

None.

Conflict of interest

George B. Stefano is the Executive Editor of this journal, but was not in any way involved in the editorial and peer-review process conducted for this paper, directly or indirectly. The author declares no conflicts of interest.

Author contributions

This is a single-authored article.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data

Not applicable.

Further disclosure

During the preparation of the perspective, the author used LLM for copy-editing purposes and is responsible for the conceptualization and factual presentation therein, as well as for producing the final copy.

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